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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,521	09/14/2004	Jean Berthier	258409US0X PCT	6722

22850 7590 03/23/2010
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EXAMINER

WILDER, CYNTHIA B

ART UNIT	PAPER NUMBER
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1637

NOTIFICATION DATE	DELIVERY MODE
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03/23/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/507,521	Applicant(s) BERTHIER ET AL.	
	Examiner CYNTHIA B. WILDER	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 February 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 September 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/18/2010 has been entered. Claim 20 has been amended. Claims 1-19 have been canceled. Claims 20-28 are pending and discussed in this Office action. Applicant's amendment necessitates the new grounds of rejections presented in this Office action. Accordingly, the rejections of the previous Office action are withdrawn.

New Ground(s) of Rejections

Claim Rejections - 35 USC § 112: New Matter Rejection

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly added amendment to claim 20, "a liquid non-foamed interface layer" is not supported by the specification as filed. While

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the specification teaches that the interface may be a liquid-liquid interface (see page 8, second paragraph). Nowhere in the specification is there a recitation of non-foamed interface layer. The specification does not support this limitation. Based on the lack of support of the instant invention as recited in the claim 20, the specification would not have suggested to the skill artisan that the Applicant was in possession of the claimed invention as of the filing date of the application.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 20-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 20-38 are indefinite in claim 20 for the step of "forming a dispersion of foam" because it is unclear how a stabilized dispersion of foam is to be formed when the interface layer is a liquid non-foamed interface layer. There doesn't appear to be clear nexus between the steps. Clarification is required.

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Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20, 22, 23, 25, 33-34 are rejected under 35 USC 103(a) as being unpatentable over Lockwood et al (Pharmaceutical Research, vol. 14, no. 11, 1997) in view of Wilde, PJ (Current Opinion in Colloid & Interface science, vol. 5, pages 176-181, 2000). Regarding claims 20, 22, 23, 25, 33 and 34, Lockwood et al teach a method for concentration of a macromolecule in a liquid sample, the method comprising: providing a liquid medium, the liquid medium comprising the liquid sample and an interface layer, wherein the interface layer located on the surface of the liquid sample, fixes the macromolecule by chemical affinity (claim 23) and has a small volume as compared to liquid sample, forming a stabilized dispersion form by injection (claim 22) directly in the liquid sample of gaseous streams to form an interstitial medium constituting the foam; and resorbing the dispersion to reform the interface layer by drainage of the interstitial medium constituting the foam, wherein the macromolecule is enriched or concentrated in the interface layer which is collected as the foamate (see entire reference, such as

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e.g., abstract and sections entitled "The Foam Fractionation process" at pages 1511 and 11512 and "solution conditions and operational parameters at page 1513). Lockwood teaches wherein the macromolecule is protein (claim 25) (abstract) and wherein the method allows for enrichment, purification and detection (claim 33 and 34) (see pages 1512 and 1513).

Lockwood et al do not expressly teach wherein the interface layer is a liquid non-foamed material. However, the use of foam and emulsion (non-foamed) are well known in the art for fractionation of macromolecules and thus the substitution for one molecule for another is within the ordinary artisan's technical grasp and further is based on the practitioner's desired results.

For example, Wilde teaches examples of foam and emulsions for formation of interface layers and their stability during dispersion (see abstract and page 176). Wilde teaches that there are two classes of surface-active molecules. Wilde teaches that the first group of surface-active molecules is surfactants which include detergents, emulsifiers and lipids. Wilde teaches that they may be water or oil soluble, and usually form a compact adsorbed layer with a low interfacial tension. Wilde teaches that the second group of surface active molecules is polymers which include amphiphilic macromolecules, the most commonly used for proteins. Wilde teaches that they typically form a visco-elastic, irreversibly adsorbed layer (page 176). Wilde teaches throughout the review different surface properties for stabilization of foams and emulsion and further provides information on how different factors effect the stabilization and interfacial properties of the surface active molecules.

Thus, given the teachings of Wilde et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention that one of ordinary skill could have substituted the foam of Lockwood for an emulsifier or lipid with a reasonable expectation of success in the method of fractionating a macromolecule as taught by Lockwood et al. The use of one surface-active molecule for another is within the ordinary artisan's technical grasp and further does not negatively affect, modify or alter the results of fractionating a macromolecule as taught by Lockwood et al in view of Wilde. Further since foam and emulsifier are within the same class of surface active molecules as taught by Wilde et al, the ordinary artisan could expect predictable results of forming an interface layer in the method of Lockwood et al.

8. Claims 21, 24, 26, 27-32, 35-38 rejected under 35 U.S.C. 103(a) as being unpatentable Lockwood et al (Pharmaceutical Research, vol. 14, no. 11, 1997) in view of Wilder, PJ (Current Opinion in Colloid & Interface science, v9l. 5, pages 176-181, 2000) as previously applied above, in view of Lalchev et al (Biotechnology and Bioengineering, vol. XXIV, pages 2253-2262, 1982) and further in view of Ijiro et al (citation made of record). Regarding claims 24, 26, 27-28, Lockwood et al in view of Wilde teach a method for enriching a macromolecule in a liquid sample, the method comprising: providing a liquid medium, the liquid medium comprising the liquid sample and an interface layer, wherein the interface layer located on the surface of the liquid sample, fixes the macromolecule and inherently has a small volume as compared to liquid sample, forming a stabilized dispersion form by injection, directly in the liquid sample of gaseous streams to form an interstitial medium constituting the foam; and

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resorbing the dispersion to reform the interface layer by drainage of the interstitial medium constituting the foam , wherein the macromolecule is enriched or concentrated in the interface layer which is collected as the foamate (see pages 15111-1513). Lockwood et al teaches wherein the macromolecule is protein, which inherently encompasses the teaching of prions, which are protein molecules (e.g., abstract).

Lockwood et al in view of Wilde do not teach wherein the macromolecule is DNA.

Lockwood et al however teaches that the method of foam fractionation can be used to separate DNA and protein (see bottom of page 1512, col. 2 bridging page 1513, col. 1). Lockwood cites Lalchev et al to support this assertion. Lalchev et al teach the successful use of foam fractionation to separate DNA and protein (see e.g., abstract and pages 2254 and 2255).

Lockwood in view of Lalchev et al do not teach wherein the method comprises specific means of fixing the macromolecule as required in the claims.

Ijiro et al. teach a method comprising forming a stabilized dispersion of an emulsion type from a medium comprising said liquid sample and an interface layer, wherein said interface is a gas-liquid interface, such as taught by Lockwood et al, said interface layer capable of fixing macromolecules (col. 2, lines 46-60; col. 3, line 35 to col. 4, line 61). Ijiro teaches wherein the fixing of the macromolecule is by chemical affinity ((col. 2, lines 46-60; col. 3, line 35 to col. 4, line 61). Ijiro et al teaches wherein the macromolecule is DNA (col. 3, lines 55-56). Likewise, Ijiro et al teaches wherein the macromolecule is DNA and the molecule capable of fixing the DNA is functionalized

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with a probe to allow specific hybridization of the DNA or an intercalator (col. 3, line 54 to col. 4, line 13).

In view of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention that one of ordinary skill in the art could obtain predictable results of enriching DNA or protein using the known methods of foam/emulsion fractionation as taught by Lockwood et al in view of Wilde in view of Lalchev et al and Ijiro et al. One of ordinary skill in the art at the time of the claimed invention would have been motivated to utilize foam/emulsion fractionation for the purpose of enriching nucleic acids or proteins or colloidal particles based on the advantages taught by Lockwood that foam fractionation has the potential to be a cost-effective component of purification/enrichment schemes (see abstract).

With regards to the claims 21, 29-32, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization of reaction components, concentrations, and parameters as evidenced by Ijiro et al. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art at the time of the claimed invention would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations and/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods using different means of mixing and fixing the DNA as claimed for the obvious benefit of detecting specific hybridization or for the benefit of controlling or detecting the

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orientation of the nucleic acid as taught by Ijiro et al (col. 7). The combination of Lockwood et al in view of Lalchev et al and Ijiro et al is *prima facie* obvious in the absence of secondary consideration.

Regarding claims 35-38, Lockwood et al in view of Wilder in view of Lalchev et al and further in view of Ijiro et al teach a method of enrichment/purification of a macromolecule, wherein the macromolecule is DNA or protein. Ijiro et al teach wherein the DNA is further used in hybridization reactions. The references do not teach wherein the DNA (macromolecule) is used in amplification reaction. However, it would have *prima facie* obvious to the ordinary artisan at the time of the claimed invention that the enriched or purified DNA or protein could be used in any of the plethora of well known biochemical reactions, such as nucleic acid amplification, sequencing, hybridization and etc. As noted earlier, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations an/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods in the absence of secondary consideration.

Response to Arguments

9. Applicant traverses the rejections on the following grounds: Applicant summarizes the instant invention and states that Lockwood procedure differs from the claimed method in several ways in that that Lockwood fails to provide a liquid non-foamed interface layer and therefore does not teach resorbing the dispersion to reform the interface layer by drainage of the interstitial film constituting the foam or by drainage of interstitial medium constituting the emulsion. Applicant states the secondary references cited therein do not meet these limitations.

10. All of the arguments have been thoroughly reviewed and considered but are not found persuasive. In response to Applicant's arguments that the reference of Lockwood et al fails to provide an interface layer, the Examiner respectfully disagrees. Firstly, the Federal Circuit discussed claim interpretation by the PTO in *In re Morris*, where the Federal Circuit noted "[A]s an initial matter, the PTO applies to the verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 44 USPQ2d 1023, 1029 (Fed. Cir. 1997). The decision of the court in *In re Bigio*, 72 USPQ2d 1209 (Fed. Cir. 2004) strongly supports the breadth of interpretation. That court noted "[T]his court counsels the PTO to avoid the temptation to limit broad claim terms solely on the basis of specification passages." In concert with *Morris* and *Bigio* is the decision in *In re American Academy of Science Tech Center*, 70 USPQ2d 1827, 1834 (Fed. Cir.

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2004), where the Federal Circuit noted "We have cautioned against reading limitations into a claim from the preferred embodiment described in the specification, even if it is the only embodiment described, absent clear disclaimer in the specification."

In this case, the specification at the bottom of page 6 bridging top of page 7 defines "interface layer" as a "monolayer (or virtually two-dimensional zone) located at the surface of the liquid sample (referred to as first liquid phase) comprising the macromolecule or the agglomerate to be concentrated. This layer, by virtue of its nature and specific properties, is able to provide the selective transfer of the macromolecule or of the agglomerate from the liquid sample to the interface layer and due to its tiny volume compared to the liquid sample, of concentrating said macromolecule or said agglomerate". Lockwood et al meets the limitations of the claims as currently written. Lockwood et al teach at page 1512, "there are two modes of operation by which foam fractionation may purify a protein, the difference lying in the relative-surface activities between the contaminants and the protein of interest". Lockwood teaches if the contaminants are more surface active, they will be removed via the foam, leaving the product in the residual solution. On the other hand, if the product of interest is more surface active, it will be enriched in the foam. Upon creation of a surface, the initial population of molecules at the interface is governed by a complex interaction of factors such as concentration, diffusivity, molecular flexibility and hydrophobicity. Lockwood teaches that due to high molecule weight, proteins are slow to adsorb, typically exhibiting diffusion control. Lockwood states that the affinity of a protein for the surface tends to be high as a result of the summed interaction of many hydrophobic force-driven

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points of attachment to the interface. Lockwood additionally depicts wherein the foamate is collected from the surface of the foam comprising the macromolecule of interest (Figure 1 and 2).

Further, Wilde provides additional examples of surface active molecules that fit in the class with foam, which includes emulsifiers and lipids. Thus, the formation of an interface layer as claimed by Applicant is within the ordinary artisan capabilities and would have been selected based on the practitioners desired results or merely routine optimization of known components (surface active molecules) capable of forming an interface layer.

Applicant's attention is directed to *KSR Int'l Co. v. Teleflex Inc.* (550 U.S._____, 127 S. Ct. 1727 (2007)) where the Supreme Court determined that "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103 (*KSR*, 550 U.S. at _____, 82 USPQ2d at 1397)." The Supreme Court also determined that "[t]he combination of familiar elements according to known methods is likely to be obvious when the combination does no more than yield predictable results (*KSR*, 550 U.S. at _____, 82 USPQ2d at 1395)." This is particularly true in this case, as the cited prior arts provide evidence that numerous surface-active molecules are capable of forming interface layer and may be used in fractionation methodologies.

Conclusion

11. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia B. Wilder/
Examiner, Art Unit 1637